



ASSOCIATION BETWEEN CHRONIC PERIODONTITIS AND SERUM LIPID LEVELS - A CROSS SECTIONAL STUDY

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ABSTRACT

Objectives: Periodontal disease is a chronic inflammatory disease inducing marked changes in the plasma concentrations of cytokines leading to a catabolic state characterized by altered lipid metabolism and hypertriglyceridemia. The main objective of the present study was to evaluate the effect of periodontal infection on serum levels of triglycerides (TGL), total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol.

Materials and Methods: A sample of 100 subjects; 50 chronic periodontitis cases and 50 periodontally healthy individuals with an age range of 25 to 55 years were included in the study. Periodontal parameters including Plaque Index, Gingival Index, Probing Depth, and Clinical Attachment Level were recorded. Venous blood samples were obtained after 12 hours fasting period from antecubital vein and serum levels of TGL, TC, HDL, and LDL cholesterol were measured.

Results: The levels of TGL, TC were significantly higher for periodontitis group ($P < 0.05$) as compared to the periodontally healthy group. HDL cholesterol levels were significantly lower in periodontitis group ($P < 0.05$) as compared to the periodontally healthy group.

Conclusion: The results of the present study indicate that periodontal disease has a definite role in altering lipid metabolism leading to hyperlipidemia. However, further studies are required to clarify the relationship between periodontitis and serum lipid levels and to determine whether periodontal therapy has the potential to reduce serum lipid levels in otherwise systemically healthy individuals.

KEY WORDS: Cardiovascular disease, cytokines, hyperlipidemia, inflammation, periodontitis

Introduction

Periodontitis is an inflammation and infection of the periodontal ligament and alveolar bone supporting the teeth that can have significant effects on general health and vice versa.¹ Various studies in the past have shown that subjects with periodontal disease may have a higher risk for cardiovascular disease.^{2,3}

Periodontal disease, as a chronic infection may be related to cardiovascular disease through infection-related mediators, hyperactivity of white blood cells, and altered lipid metabolism leading to hyperlipidemia.²

A high serum lipid level is one of the modern society concerns. Hyperlipidaemia is a condition wherein there is an elevation of the serum levels of total cholesterol (TC) and triglycerides (TGL) due to alteration of lipid metabolism, with an increase in the liver lipogenesis and lipolysis in the adipocytes.⁴

It has been shown that systemic exposure to infectious challenges such as bacterial lipopolysaccharide can alter fat metabolism and promote hyperlipidemia.⁵ *P. gingivalis* has shown to invade deep connective tissues/vascular endothelium associated with the periodontium and can be found within vascular pathological plaques, eliciting a circulating antibody response.⁶ Thus, it can be stated that a relationship exists between chronic periodontitis and hyperlipidemia that involves the inflammatory response to LPS from periodontal pathogens such as *Porphyromonas gingivalis*.⁵

The association between altered lipid profile and periodontitis has also been investigated in several studies.^{5,7}

The results of these studies, however, are somewhat inconsistent. Therefore, considering the diversity of the few developed studies, as well as the different eating habits and studied populations, researches to establish the real systemic changes caused by periodontitis are needed in order to explain the metabolic and/or physiological changes responsible for changes in general health and the increased susceptibility for certain systemic diseases. Hence, the purpose of the present study was to assess the relation between chronic periodontal disease and the serum levels of total cholesterol, low, very low and high density lipoproteins (LDL, VLDL, HDL) and triglycerides.

Materials and methods

Source of data

The study was conducted in the Department of Periodontology, Terna Dental College and Hospital. 100 subjects were selected for this study from the Outpatient Department of Periodontics and were divided into the test and control groups.

Test group (Group A) - Included 50 patients with chronic periodontitis

Control group (Group B) - Included 50 periodontally and systemically healthy individuals.

Inclusion criteria for the chronic periodontitis group-

- Patients between the age group of 25 – 55 years.
- Patients who readily gave informed consent for the study.
- Patients who had more than 3 sites with a minimum clinical attachment loss (CAL) of 1mm
- Radiographic evidence of bone loss present.

Exclusion criteria-

- Any other systemic diseases affecting lipid metabolism (i.e. rheumatoid arthritis, diabetes mellitus or other endocrine diseases, nephritic syndrome, chronic renal disease, and cardio-vascular disease)
- Obese individuals with body mass index more than 25.⁸
- Patients having received any periodontal treatment in the past 6 months,
- Any systemic antibiotic administration within the last 3 months.
- Known hyperlipidaemic patients undergoing medical treatment
- Smokers
- Pregnant Women and Lactating mothers.

Study design

Ethical approval for the study was obtained from the Institution ethics committee. All the participants were informed in detail about the procedure and an informed signed consent was obtained from them. A detailed case history of subjects was taken. The following clinical and radiological parameters were recorded for periodontal disease assessment for all the patients-

- Plaque Index (Sillness and Loe)⁹
- Gingival Index (Loe & Sillness)¹⁰
- Clinical attachment level
- Russell's Periodontal Index¹¹

Patients were called after a 12 hour fasting period. Venous blood samples were obtained for the assessment of lipid profile (triglycerides, total cholesterol, VLDL, LDL-C, and HDL-C levels). 5 ml of venous blood was obtained from the antecubital vein and transferred into transparent vials. The blood samples were immediately transported to the pathology laboratory of Terna Sahyadri Hospital wherein the fasting serum lipid levels were evaluated.

TC and HDL cholesterol levels were determined by the End Point method under the principle of enzymatic determination of TC using the following reactions. Cholesterol ester is converted into cholesterol and fatty acids in the presence of cholesterol esterase. Cholesterol is oxidized in the presence of cholesterol oxidase to produce hydrogen peroxide. Hydrogen peroxide reacts with Phenol and 4-Aminoantipyrin in the presence of peroxidases to give Quinone and water molecule to produce red color. The intensity of color developed is proportional to the concentration of TC and HDL.

TGL were determined by GPO (Glycerophosphate oxidase)/POD (Peroxidase) method. TGL are hydrolyzed by lipase to glycerol and free fatty acids. Glycerol is phosphorylated by ATP in the presence of glycerol kinase to Glycerol-3-phosphate which is oxidized by the enzyme Glycerol-3-phosphate oxidase producing hydrogen peroxide. Hydrogen peroxide so formed reacts with 4-Aminoantipyrine and 4-Chlorophenol in the presence of enzyme peroxidases to produce red Quinoneimine. The intensity of color developed is proportional to the TGL concentration.¹²

LDL cholesterol was assessed according to the formula by Friedewald et al. in 1972, in which $LDL = TC - (HDL + TG/5)$.¹³

In this formula, TG/5 gives a measure of VLDL cholesterol because VLDL carries most of circulating TG. Hence in the study VLDL was assessed using the above mentioned formula.

Cut off points were taken as follows:

- TC- more than or equal to 250 mg/dl
- HDL- less than or equal to 65mg/dl
- TGL- more than or equal to 160 mg/dl
- LDL- more than or equal to 130 mg/dl
- VLDL- more than or equal to 40 mg/dl

Data collection and statistics:

All the findings of this study were tabulated and statistically analyzed using SPSS version 17 software.

Results-

The total study population consisted of 100 participants (58 males and 42 females) within the age group of 25 to 55 years who fulfilled the inclusion criteria. The 100 participants were then divided into two groups i.e. Group A (50 patients with chronic periodontitis) and Group B (50 periodontally healthy subjects). Both groups i.e. Group A and Group B comprised of 29 males and 21 females each respectively. The selected subjects were explained about the details of the study and an informed consent was obtained from them. The demographic data, periodontal parameters, and serum lipid profile were obtained. The obtained data was statistically analyzed using Microsoft Excel and Statistical software (SPSS version 17). For all these tests, a P value of 0.05 or less was set for statistical significance (S).

Lipid parameters between chronic periodontitis (Group A) and periodontally healthy subjects (Group B) were compared using the unpaired T test. Pearson correlation coefficient (r) was used to describe the correlations between age, lipid parameters, and periodontal parameters.

Significant differences were found when comparison of TC (P=0.0), HDL (P=0.0), VLDL (P=0.0), TG (P=0.0) was done between Group A and B. (Table 1)(Figures 2,3,5,6) However, the difference for serum LDL (P=0.4) was found to be non-significant between the two groups. (Table 1)(Figures 1 and 4)

When comparison of lipid parameters between age, gender, within Group A and Group B was done, the differences were only significant for VLDL (P=0.05) and TG (P=0.04) in Group A and for TC (P=0.01), LDL (0.02), TG (0.01) in Group B as depicted in table.2.

When comparison of lipid parameters with GI and PI was done within Group A and B, none of the parameters were significant as depicted in table 3. However, when the various lipid parameters were correlated with the clinical attachment loss, it was seen that there was significant relationship between the elevated lipid levels and periodontal disease except for serum.

When comparison of lipid parameters between males and females between Group A and B was done, none of the parameters were found to be significant, except within Group A, the difference between male and female lipid parameters were significant for VLDL and TG as depicted in table 4.

Discussion-

For many years, the prevailing view was that periodontal infections were localized only to the periodontium and rarely had any systemic implications in healthy

individuals. However, recent evidence has shown that periodontitis is known to induce increased systemic inflammation.¹⁴

A significant association between periodontitis and elevated serum lipid levels has been reported in various studies carried out previously.^{5,15} However, the prevalence of hyperlipidemia is still scarcely established, and the results of the studies are controversial. Hence, this study was designed for better understanding of the association between periodontal disease and serum lipid levels.

Hundred systemically healthy subjects within the age range of 25 to 55 were included in the study. Fifty eight males and forty two females participated in the study. The mean age of participants in the chronic periodontitis group was 45 years and in the periodontally healthy group was 42 years respectively.

The body mass index of all participants in the study was less than 25. This suggests that the subjects were in the normal weight range.¹⁶ Thus, the potential effect of obesity on lipid profile of the participants was eliminated.

In the present study, we found that the serum levels of TC, VLDL, TG were significantly higher in the chronic periodontitis group as compared to the periodontally healthy group after eliminating potential confounders such as the patient's physical activity, habits, socio-economic conditions, obesity, age, stress, and geographical location. This increase in lipid levels in the chronic periodontitis group might be attributed to the increased severity or the presence of pro-inflammatory cytokine production in the chronic periodontitis group compared to the periodontally healthy subjects.

Periodontal disease results in repeated systemic exposure to bacteria, endotoxins, lipopolysaccharide and other bacterial products. The lipopolysaccharides of dental plaque diffuse into the systemic circulation and they elicit a systemic lipopolysaccharide specific antibody response. This leads to a disturbance in lipid metabolism and a hypercoagulable state through elevation of circulating cytokines.

Plasma TGL levels increase from increased VLDL secretion as a result of adipose tissue lipolysis, increased de novo hepatic fatty acid synthesis, and suppression of fatty acid oxidation.

IL-1 β and TNF- α are known to exert an effect on lipid metabolism by influencing the production of other cytokines, altering hemodynamics/ amino acid utilization of various tissues involved in lipid metabolism, or modifying the hypothalamic-pituitary-adrenal axis increasing plasma concentrations of adrenocorticotrophic hormone, cortisol, adrenaline, noradrenaline, and glucagon.¹⁵

Thus in our study, the serum lipid levels of TC, TG, VLDL were found to be higher in the chronic periodontitis group as compared to the periodontally healthy group.

HDL cholesterol has anti-inflammatory and anti-atherogenic properties and decreased HDL cholesterol levels have also been considered to be a risk factor for CVD. In our study, serum HDL values were significantly lower in the periodontitis group compared with periodontally healthy subjects.

The results of the present study are in accordance to those of the studies conducted by Cutler et al in 1999, Loesche et al in 2000, wherein they found that the serum lipid values in patients with chronic periodontitis were significantly higher than the subjects in the control group.^{5,7}

However, contradictory results have been found in studies conducted by Loos et al in 2002, Machado et al in 2005, Valentavicius et al in 2005 wherein they found no significant difference in blood lipid levels between patients with chronic periodontitis and the periodontally healthy or the gingivitis group.^{18,19,20}

In these studies, the results may have been influenced by the fact that they did not take into consideration other aspects such as physical activity, nutrition and stress of the participants.¹⁹

In the study by Loos et al in 2000, no rise in the levels of TGL and cholesterol were observed in periodontitis group when compared to control group. This could be due to the fact that non-fasting venous blood was obtained in the study which might have altered the plasma lipid values.¹⁸ In our study, blood was drawn after a 12 hour fasting period as food intake is known to alter the serum TGL levels.

Another important reason for the discrepancy among the results of these studies could be due to the difference in severity of periodontitis in individuals assigned to case groups. These studies have taken into consideration subjects with mild, moderate as well as severe periodontitis which accounts for the variability in the results of these studies.

In the present study, only the difference in the mean LDL values between the two groups was not statistically significant. This could be due to the variation in dietary pattern of the various participants which may have affected the results along with certain unknown socioeconomic conditions.

Similar results were obtained by Moeintaghvi et al in 2005 where in they found that the levels of LDL cholesterol were higher in patients with chronic periodontitis but did not have any significant differences with controls. In this study by Moeintaghvi et al in 2005, the patients' diet and physical activity patterns were not taken into consideration.

When lipid profile between male and female subjects was compared in both the groups, none of the parameters were found to be significant, except within the chronic periodontitis group, wherein the difference between male and female lipid parameters were significant for VLDL and TG. These levels were more in males compared to female subjects. These differences could be attributed to the variation in genetics and hormonal influences between male and female subjects. When similar comparison was done within the periodontally healthy group, the difference in the lipid parameters between males and females was found to be statistically insignificant. This shows the lack of consistent pattern observed for serum lipid levels between male and female subjects.

The results of our study demonstrated a positive correlation between clinical attachment loss with TGL, TC, VLDL and a negative correlation with HDL values. This shows that with increasing CAL, the values of TGL, TC, and LDL increased but the value of HDL decreased.

This is in accordance with the study conducted by Katz et al. who hypothesized that there is a strong positive statistical association between loss of attachment and serum lipid levels, thereby confirming a positive relationship between periodontitis and hyperlipidemia.

However, in our study, there was no significant association of serum LDL with clinical attachment loss. This result is in line with the study conducted by D'Autio et al in 2004 where they found no significant correlation between serum LDL and periodontal disease. From all the above observations, an important question which needs to be addressed is whether periodontitis should be aggressively treated as a preventive measure for cardiovascular disease.

In a preliminary intervention study, D'Autio et al in 2004 showed that non-surgical periodontal treatment led to a reduction in serum CRP (C reactive protein) and IL-6, thus decreasing the overall inflammatory response.²⁴ This suggested a potential dose-response effect between the extent of resolution of the local periodontal infection and the level of reduction in systemic inflammation.

To conclude, the disagreement observed in the various studies that relate periodontal disease with hyperlipidemia may be in part due to

- A great number of confounding variables such as diet and physical activity habits, socio-economic conditions, obesity, age, stress, which are factors subjected to the environment in which the individual lives, interfering with the study results.
- The methods of assessing periodontitis, namely, based only on-
- Clinical measures like bleeding on probing, clinical attachment level, and probing depth; and
- Non-clinical measures like systemic antibody response, alveolar bone levels, and carotid artery intimal-medial thickness.

Again, even, though numerous studies with conflicting results are presented in the literature, there is still no concrete evidence which determines if periodontitis is an independent risk factor for atherosclerotic CVD.

Limitations of the study-

- The drawback of the present study was that the socio-demographic characteristics such as age, educational level, patients' physical activity, habits, were self-reported. Thus, some participants could have misreported resulting in a bias in our results.
- Also, the patients' dietary pattern was not recorded which could have influenced the results of the study by acting as a confounding factor.
- The study participants submitted blood samples for assessment of the lipid profile only once. Hence, there are likely to be intra-individual variations in lipid levels which were not considered in the study.

Conclusion-

The present study indicates that periodontal infection has a definite role in altering lipid metabolism which supports the hypothesis that there exists a relationship between chronic periodontitis and hyperlipidemia.

Based on the results of our study and after eliminating the potential confounding factors such as patient's physical activity, habits, socio-economic conditions, obesity, age, stress, and geographical location, the following conclusions can be drawn:

- There is a significant association between periodontitis and hyperlipidemia.
- However, it is not clear yet whether the observed changes in lipid metabolism are the cause or the consequence of periodontal disease.
- Thus, periodontitis and cardiovascular disease may share common risk factors, and the association between periodontitis and coronary heart disease may be due to the elevated levels of plasma lipids.

From the present study, we can conclude that there exists a positive association between periodontitis and elevated blood lipid levels. However, further investigations with a better study design are still needed for better exploration of the relationship between periodontitis and serum lipid levels and also to determine whether oral healthcare has the potential to reduce serum lipid levels in otherwise systemically healthy individuals.

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